POOR LEGIBILITY

ONE OR MORE PAGES IN THIS DOCUMENT ARE DIFFICULT TO READ
DUE TO THE QUALITY OF THE ORIGINAL

(p. 922) refer to the treatment of routine cases in which no particular complication was anticipated, and they lay stress on reinfection as the chief problem in recurrent cases. I wish to draw attention to the value of metronidazole in cases of trichomonal infestation of the vagina which have proved altogether resistant to local therapy, and in which reinfection is unlikely to have taken place. Two such patients have recently been cured (apparently) by this oral therapy after three and three and a half years respectively of almost uninterrupted and largely unavailing local treatment.

A single woman, aged 36, was found to have trichomoniasis of the vagina immediately following hysterectomy. She was treated successively with the following: "penotrane" pessaries, acetarsol pessaries inserted through a speculum, vaginal swabbing and packs, "aroxine" pessaries, "floraquin" pessaries, "penotrane" cream, further packs as an in-patient, floraquin pessaries (4 nightly), tampons, oestrogen, penotrane detergent swabbing, carbarsone pessaries, "sterisil" jelly, carbarsone (double dosage), "iodevan" swabbing, acetarsol pessaries, surgical toilet, "aci-jel" jelly, "triple sulfa cream," "dequadin" pessaries, "terramycin" pessaries, proflavine pessaries and mercurochrome swabbing. She worked as an orderly in hospital and swabs were sent regularly for laboratory examination, but although some forms of treatment gave temporary symptomatic improvement the trichomonads never disappeared from the vagina. Eventually metronidazole was used, 200 mg. being taken orally thrice daily for 14 days (double the recommended course), and, although the patient was reluctant to admit much benefit, the vaginal discharge showed only a few scanty trichomonal organisms. In view of the chronicity of the infection a further course of 200 mg. t.d.s. was given for three more weeks with the use of acetarsol vaginal pessaries as well. Relief was immediate and swabs have remained negative for two months.

The other patient was aged 25 when seen with a vaginitis that occurred during her third puerperium, and which commenced as a mixed infection of monilia and trichomonads. She was treated unsuccessfully with 14 different types of vaginal therapy, and a course of oral aminitrazole. Reinfection could not be entirely excluded, but seemed highly improbable. Temporary benefit occurred after the use of carbarsone pessaries and also after swabbing twice weekly with 10% mercurochrome. In view of the chronicity of the infection she was given a double course of metronidazole (200 mg. t.d.s. for 14 days), and was apparently cured. It is too early to exclude relapse, but the response was dramatic.

It is worthy of note that the first of these patients had been regarded as a psychiatric problem in view of her unsatisfactory emotional state, and it had been questioned more than once whether she did, in fact, wish to be cured of her vaginal discharge. The dramatic improvement in personality as soon as she found herself free from discharge for the first time in almost four years made her attendants realize how much emotional distress may be caused by chronic vaginitis.

The metronidazole ("flagyl") was very kindly supplied by Dr. R. Forgan, of Messrs. May and Baker Ltd.

—I am, etc.,

Birmingham. WILFRID MILLS.

New Rashes for Old

SIR,—We have just had a localized epidemic in this practice of the febrile illness and rash described by Dr. Joan B. Landsman and her colleagues (August 6, p. 464) and by Dr. J. Parton (August 27, p. 665). Seventeen children were affected and five of their parents, all living on the same housing estate. The rash was blotchy, pink, and papular on the face, maculo papular and suggestive of measles or rubella on th body. A third element, a transient confluent erythem in the groin, was noted in two cases.

One boy got virus meningitis on the fifth day, whic first suggested that we might be dealing with the sam illness as Dr. Landsman. All the others recovere within a week, the rash lasting between one and fou days. Of the five parents affected, only one had th rash, the others complaining of sore throat, headache and aching in the back and limbs, "like 'flu." The olde children complained of sore throat and headache, whil the younger were fretful with vomiting and loose stool Two young children had cough and coryza, in on severe enough to suggest measles.

The Newcastle Virus Laboratory has isolate E.C.H.O. virus type 9 from the stools of five of th cases, including the boy with meningitis and two of th parents who had the illness without the rash.—We are etc.,

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ANDREW SMITH.
DEREK BELL.
DAVID F. SMITH.
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Newcastle upon Tyne.

Potassium Perchlorate in Thyrotoxicosis

SIR,—Your thoughtful leading article on potassium perchlorate in thyrotoxicosis (August 13, p. 517) mentions but does not perhaps sufficiently stress th rather remarkable relationship between the dose of thi drug and the incidence of side-effects. This relationship emerged very clearly from the studies of Crooks and Wayne[1] in Glasgow. A recent review of our own patients shows that the incidence of all types of side-effects (taken together) is astonishingly similar in their clinic and ours, not only with potassium perchlorate bu also with two other antithyroid drugs. The actual figures are given below:

Drug	Dose	Crooks and Wayne		Morgans and Trotter	
	mg./Day	No. of Patients	Toxic Reactions (%)	No. of Patients	Toxic Reactions (%)
Potassium perchlorate	400–1,000	200	2	180	3
Potassium perchlorate	1,200–2,000	50	16	67	18
Carbimazole ..	20–60	85	8	57	10
Methyl thiouracil	200–600	151	7	358	9

The close correspondence between the Glasgow and London series enables them to be combined for significance tests. These show that the smaller doses of perchlorate were associated with fewer toxic reactions than carbimazole or methyl thiouracil; whereas the larger doses of perchlorate were associated with more frequent toxic reaction than methyl thiouracil ($P<0.0$ in all cases). By the same criterion, large doses of perchlorate caused more reactions than small doses of perchlorate in both series, considered separately.

The 12 reactions in our patients treated with the large doses (1,200 or 1,600 mg. daily) of perchlorate consisted of two cases of rash with fever, eight cases of rash alone, and two cases of lymphadenopathy. These are similar in type to the reactions observed by Crooks and Wayne, and can be regarded as manifestations of hypersensitivity. The reactions of this type are thought of as responses to a drug protein complex which is acting as an antigen, the followin

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hypothesis may be put forward as a possible explanation of the marked relationship between the incidence of reactions and the dose of perchlorate. Let us suppose that perchlorate may become attached to one or both of two possible binding-sites within the body. One of these (A) has a greater binding affinity for perchlorate, and the complex formed is non-antigenic. The other (B), with a lesser affinity, only binds perchlorate when the capacity of the first binding-site is saturated. Perchlorate will only become bound to B when large doses are given, or in individuals with a reduced amount of A-type binding-sites. Only when perchlorate is attached to B is the resulting complex antigenic.

Whatever the theoretical explanation, it would seem advisable to take note of the close dependence of toxic reactions upon perchlorate dosage. It is likely that the only serious toxic effect—agranulocytosis—would be equally dependent upon dosage. Fortunately the instances of this complication so far reported are too few in number for direct verification of this supposition. Crooks and Wayne's case[1] was receiving 1,500 mg. daily, and Southwell and Randall's case[2] 1,000 mg. daily. To these we can add a third (unpublished) case seen by Dr. Harold Lambert at this hospital, in which a woman developed a severe leucopenia within two weeks of starting perchlorate in a dose of 1,600 mg. daily (this patient is not included in our series).

Our own previously published recommendations about perchlorate dosage are now seen to have been consistently wrong. In 1954 we were using 400 mg. daily,[3] a dose which is clearly too small to be effective in many cases. In 1957 we increased the dose to 1,600 mg. daily,[4] with the result that we are now able to confirm Crooks and Wayne's finding that doses of this order are highly toxic. A reasonable compromise would therefore seem to be to use doses in the region of 800 mg. daily.—We are, etc.,

M. E. MORGANS.
W. R. TROTTER.

University College Hospital Medical School, London W.C.1.

REFERENCES

1 Crooks, J., and Wayne, E. J., *Lancet*, 1960, **1**, 401.
2 Southwell, N., and Randall, K., ibid., 1960, **1**, 653.
3 Morgans, M. E., and Trotter, W. R., ibid., 1954, **1**, 749.
4 —— —— ibid., 1957, **2**, 1173.

Hypophysectomy in Breast Cancer

SIR,—Mr. M. A. Falconer and Mr. J. L. Hayward in a recent letter (September 17, p. 856) ask me to give the evidence on which certain statements in my Oliver-Sharpey Lectures are based. Briefly they may be summarized as follows:

(1) "That it is doubtful whether it is justified to undertake surgical hypophysectomy in patients with advanced breast cancer."

(*a*) It involves a major operation on a patient who has often had a major operation shortly before. Nearly all patients dislike the idea of a craniotomy. (*b*) The operation is not a cure, only 50% of patients can anticipate a temporary remission perhaps lasting one to two years. (*c*) Psychological changes may follow surgical hypophysectomy. (*d*) Diabetes insipidus developed in about half our cases and has lasted up to three years. (*e*) As Atkins *et al.*[1] point out, widespread introduction of surgical hypophysectomy for advanced breast cancer is impracticable in terms of neurosurgical man hours.

(2) That yttrium-90 implantation seems to have advantages over surgical hypophysectomy and bilateral adrenalectomy and that the Glasgow screw-in method is the best so far developed.

(*a*) It is a relatively minor procedure. (*b*) It is an effective method of pituitary destruction (Section of Endocrinology, Royal Society of Medicine. Discussion on the assessment of endocrine function after hypophysectomy or pituitary destruction, October 28, 1959). (*c*) It is relatively free from side-effects—the figure of 10% quoted by Mr. Falconer and Mr. Hayward for C.S.F. rhinorrhoea is incorrect; with the latest reported method it is 1 in 43.[2]

(3) Replacement therapy after adrenalectomy is undoubtedly simpler than after hypophysectomy.

After hypophysectomy not only must cortisone or a similar steroid be given but also thyroid replacement and in about 50% of cases pitressin. We have not found the snuff very satisfactory, and usually intramuscular injections of pitressin tannate in oil are required. The diabetes insipidus has given our hypophysectomized patients a lot of trouble. It should perhaps be mentioned that Mr. Valentine Logue, the neurosurgeon who performed these operations, has not clipped or coagulated the pituitary stalk. It has been cleanly divided.

—I am, etc.,

London W.1. JOHN NABARRO.

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1 Atkins, H. J. B., Falconer, M. A., Hayward, J. L., MacLean, K. S., Schurr, P. H., and Armitage, P., *Lancet*, 1960, **1**, 1148.
2 Section of Endocrinology, Royal Society of Medicine, *Proc. roy. Soc. Med.*, 1960, **53**, 81.
3 Forrest, A. P. M., Blair, D. W., Valentine, J. M., and Sandison, A. T., *Lancet*, 1959, **2**, 971.

Medical Practice Centre

SIR,—Your Special Hospital Number (September 10) prompts me to cry out the needs of the Cinderella of the profession—general practice—which I cannot remember being given so generous a coverage.

To state the obvious: The practitioner's aim is to make the patient feel "at home" while devoting as much time and careful attention as possible to the history and examination, and then to the giving of advice. Unfortunately the interruptions of the telephone, the agony of waiting for an unwell person to undress and dress, while aware of a full waiting-room, inefficient filing systems, and so forth, can make us fall far short of our aim. Indeed, many efficiency factors enter into general practice—layout of accommodation, employment of ancillary help, types of furniture and equipment, to mention a few—which have no relation to the medical curriculum. One frequently finds that ex-trainees have not been recommended books on these matters, although there exists, for example, the Nuffield report *Good General Practice* by Lord Taylor.[1]

I feel there should be set up a Medical Practice Centre, which can advise on organization and methods in general practice. It should have a wide remit; its information be as well indexed as that of the Design Centre; the frequently changing exhibitions as comprehensive as those of the Building Centre. There should be peripatetic advisers, as offered, for example, by the Medical Insurance Agency, and the whole should be administered by the profession. To finance such a scheme on a realistic scale would require large capital, and perhaps one of the Trust Funds would be willing to help. Such a centre would assist us in raising our standards and would enable us to provide the best possible general medical service to the public.—I am, etc.,

London N.W.3. R. LAW.

REFERENCE

1 Taylor, S., *Good General Practice*, 1954. Oxford Univ. Press, London.